Dept. Genetics, University of Wisconsin, Madison 6, Wis., U.S.

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Dear Dr. Scholtens:

I should be very pleased to discuss the speculations on bacteriophage mentioned in your letter and papers.

That a bacteriophage is a parcel of genetic material is, I think, beyond doubt. The question is to what extent the host bacterium carries its own genetic determinants (in a nucleus?) independently of the bacteriophage. My own thinking on this question is that symbiosis adequately conveys the concepts of the relationships between phage and bacterium. If one focusses attention on the symbiotic complex, there are of course many traits that are governed by the phage component.

To my mind, one can draw quite opposite conclusions than those expressed by Doerr from the phenomenon of lysogenicity. The fact that a previously sensitive bacterium can become lysogenic by infection with an exogenous phage shows that the theory of phage as a viral parasite (or symbiont) is adequate to explain the occurrence of lysogenic bacteria. The induction of lysogenicity is perhaps not so clearcut in the Salmonella group as, for example in E. coli or in staphylococci, but so far as I can see, only because of the prevalence of lysogenicity in this group. I will admit the possibility that the phage-bacterium complex may evolve in the direction of obligate symbiosis, but there is no clearcut evidence that this has happened, and until this is proven, I feel that the concept of the complex as an association of two organisms remains more utilitarian. When this complex is as characteristic as it is in the Salmonellae, there is considerable virtue in basing a practical classification (for epidemiological purposes) on it.

Although I could not honestly insist on a final proof, I do not feel that we should identify FA with the phage that provokes it. Most important by way of evidence, the genetic capacities of FA are determined by the bacterium from which it is produced, not the phage which elicited it. For example, a phage from a streptomycin-sensitive lysogenic bacterium provokes FA for the trait streptomycin-resistance when resistant bacteria are grown in the presence of such phage. On the other hand, phage from a resistant bacterium does not provoke "resistance-FA" from bacteria sensitive to streptomycin. Of course, you can argue if you wish that the properties of the phage are directly modified by the bacterium on which it is grown; I would say that if the phage plays any direct role at all it is at most the vehicle of FA, not the immediate source of its specificity, which comes from the bacterium, If the phage itself has genetic properties usually associated with the bacterium these should be propagated more consistently when the phage is grown on different hosts. This point can be illustrated by other examples that will be familiar to you: for example, the Lisbonne- Warrere strain of E. coli produces a bacteriophage active against rough Shiga bacteria. Lysogenic Shiga can be secured by the action of the phage but these do not therefore show traits of the E. coli except for the phage itself

The behavior of FA is itself so surprising that I would not wish to be dogmatic about its relationships. But my own conclusions for the present are in favor of the parasitic-virus theory of bacteriophage, admitting that this type of association may well evolve into something more subtle.

Yours sincerely,

Joshua Lederberg
Associate Professor of Genetics